

2. **(Reiterated)** A method for inhibiting the growth of a lung tumor which expresses hedgehog, comprising contacting the lung tumor with an amount of an agent effective to inhibit the growth of the lung tumor, wherein the agent is selected from a *hedgehog* antagonist, a *ptc* agonist, and an *fgf-10* antagonist.

3. **(Twice Amended)** The method of claim 33, wherein the lung cancer tissue is in culture, and the *hedgehog* antagonist is provided as a cell culture additive.

4. **(Reiterated)** The method of claim 1, wherein the cell is treated in an animal and the agent is administered to the animal as a therapeutic composition.

5. **(Reiterated)** The method of claim 1 or 2, wherein the agent is a *hedgehog* antagonist.

6. **(Reiterated)** The method of claim 5, wherein the *hedgehog* antagonist is a polypeptide including a *hedgehog* polypeptide sequence of at least an extracellular portion of a *hedgehog* polypeptide that binds to a *patched* polypeptide and blocks *hedgehog* signaling.

7. **(Amended)** The method of claim 6 or 33, wherein the polypeptide includes at least 50 amino acid residues of an N-terminal half of the *hedgehog* polypeptide.

8. **(Amended)** The method of claims 6 or 33, wherein the polypeptide includes at least 100 amino acids of an extracellular domain of the *hedgehog* polypeptide.

9. **(Amended)** The method of claim 6 or 33, wherein the polypeptide includes at least a portion of the *hedgehog* polypeptide corresponding to a 19 kd fragment of an extracellular domain of the *hedgehog* polypeptide.

10. **(Amended)** The method of claim 6 or 33, wherein the *hedgehog* polypeptide is encoded by a nucleic acid of a vertebrate organism.

11. **(Amended)** The method of claim 6 or 33, wherein the polypeptide includes a *hedgehog* polypeptide sequence represented in the general formula of SEQ ID No: 21.

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12. (Amended) The method of claim 6 or 33, wherein the polypeptide includes a *hedgehog* polypeptide sequence represented in the general formula of SEQ ID No: 22.

13. (Amended) The method of claim 6 or 33, wherein the *hedgehog* polypeptide is encoded by a human *hedgehog* nucleic acid.

14. (Amended) The method of claim 6 or 33, wherein the *hedgehog* polypeptide sequence is at least 70 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.

15. (Amended) The method of claim 6 or 33, wherein the *hedgehog* polypeptide sequence is encodable by a nucleic acid sequence which hybridizes under stringent conditions, including a wash step of 0.2X SSC at 65 °C, to a sequence selected from SEQ ID No:1, SEQ ID No:2, SEQ ID No:3, SEQ ID No:4, SEQ ID No:5, SEQ ID No:6, SEQ ID No:7, SEQ ID No:8, SEQ ID No:9, and SEQ ID No:19.

Rebuttal

22. (Reiterated) The method of claim 1 or 2, wherein the *hedgehog* antagonist, *patched* agonist, or *fgf-10* antagonist is a small organic molecule.

23. (Reiterated) The method of claim 5, wherein the *hedgehog* antagonist is a small organic molecule.

24. (Reiterated) The method of claim 5, further comprising preparing a formulation including an identified *hedgehog* antagonist and a pharmaceutically acceptable excipient.

Rebuttal

25. (Reiterated) The method of claim 5, wherein the *hedgehog* antagonist binds to *hedgehog* and blocks *hedgehog* signal transduction.

26. (Reiterated) The method of claim 5, wherein the binding of the *hedgehog* antagonist prevents the upregulation of *patched* and/or *gli* expression.

27. **(Reiterated)** The method of claim 5, wherein the *hedgehog* antagonist decreases *hedgehog* signal transduction by altering the localization, protein-protein binding and/or enzymatic activity of an intracellular protein involved in a *hedgehog* signal transduction pathway.

28. **(Reiterated)** The method of claim 5, wherein the *hedgehog* antagonist alters the level of expression of a *hedgehog* protein, a *patched* protein or a protein involved in a *hedgehog* signal transduction pathway.

29. **(Reiterated)** The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 75 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.

30. **(Reiterated)** The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 85 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.

31. **(Reiterated)** The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 90 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.

32. **(Reiterated)** The method of claim 6, wherein the *hedgehog* polypeptide sequence is at least 95 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.

Please add the following new claims:

33. (New) A method for inhibiting at least one of the proliferation and growth of lung cancer cells which express *hedgehog*, comprising contacting the cells with an amount of a *hedgehog* antagonist effective to alter the proliferation or growth of the lung cancer cells, wherein the *hedgehog* antagonist is a polypeptide including a *hedgehog* polypeptide sequence of at least an extracellular portion of a *hedgehog* polypeptide that binds to a *patched* polypeptide and blocks *hedgehog* signaling.

34. (New) A method for inhibiting at least one of the proliferation and growth of lung cancer cells which express *hedgehog*, comprising contacting the cells with an amount of a *hedgehog* antagonist effective to alter the proliferation or growth of the lung cancer cells, wherein the *hedgehog* antagonist is a small organic molecule.

35. (New) The method of claim 33 or 34, further comprising preparing a formulation including an identified *hedgehog* antagonist and a pharmaceutically acceptable excipient.

36. (New) The method of claim 1, wherein the *hedgehog* antagonist is a *hedgehog* antibody.

*The amended claims are restated below to reflect changes from the last filing.*

1. (Thrice Amended) A method for inhibiting *in vivo* at least one of the proliferation and growth of lung cancer cells which express *hedgehog*, comprising contacting the cells with an amount of an agent effective to alter the proliferation or growth of the lung cancer cells, wherein the agent is selected from a *hedgehog* antagonist, a *ptc* agonist, and an *fgf-10* antagonist.

3. (Twice Amended) The method of claim 1 or 33, wherein the lung cancer tissue is in culture, and the agent *hedgehog* antagonist is provided as a cell culture additive.

7. (Amended) The method of claim 6 or 33, wherein the polypeptide includes at least 50 amino acid residues of an N-terminal half of the *hedgehog* polypeptide.

8. (Amended) The method of claims 6 or 33, wherein the polypeptide includes at least 100 amino acids of an extracellular domain of the *hedgehog* polypeptide.
9. (Amended) The method of claim 6 or 33, wherein the polypeptide includes at least a portion of the *hedgehog* polypeptide corresponding to a 19 kd fragment of an extracellular domain of the *hedgehog* polypeptide.
10. (Amended) The method of claim 6 or 33, wherein the *hedgehog* polypeptide is encoded by a nucleic acid of a vertebrate organism.
11. (Amended) The method of claim 6 or 33, wherein the polypeptide includes a *hedgehog* polypeptide sequence represented in the general formula of SEQ ID No: 21.
12. (Amended) The method of claim 6 or 33, wherein the polypeptide includes a *hedgehog* polypeptide sequence represented in the general formula of SEQ ID No: 22.
13. (Amended) The method of claim 6 or 33, wherein the *hedgehog* polypeptide is encoded by a human *hedgehog* nucleic acid.
14. (Amended) The method of claim 6 or 33, wherein the *hedgehog* polypeptide sequence is at least ~~60~~ 70 percent identical to an amino acid sequence of a *hedgehog* protein selected from SEQ ID No: 10, SEQ ID No:11, SEQ ID No:12, SEQ ID No:13, SEQ ID No:14, SEQ ID No:15, SEQ ID No:16, SEQ ID No:17, SEQ ID No:18, and SEQ ID No:20.
15. (Amended) The method of claim 6 or 33, wherein the *hedgehog* polypeptide sequence is encodable by a nucleic acid sequence which hybridizes under stringent conditions, including a wash step of ~~2-4~~ 0.2X SSC at ~~50~~ 65 °C, to a sequence selected from SEQ ID No:1, SEQ ID No:2, SEQ ID No:3, SEQ ID No:4, SEQ ID No:5, SEQ ID No:6, SEQ ID No:7, SEQ ID No:8, SEQ ID No:9, and SEQ ID No:19.